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EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,466	TAYLOR ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11,21,26-28 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11,21,26-28 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 5/10/04. Claims 3, 12-20, 22-25 and 29-32 have been cancelled. Claims 1, 7, 10-11, 21 and 26-28 have been amended. Claims 1-2, 4-11, 21, 26-28 and 33 are pending in the application.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are new grounds of rejection herein that were not necessitated by Applicant's Amendment and therefore, this action is non-final.

Claim Objections

Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 5 recites that the RNA is separated from the agent by MIPC and is dependent upon claim 1. Claim 1 has been amended to recite that the RNA is degraded by MIPC.

Claim 26 is objected to because of the following informalities: Claim 26, line 1-4 recites that the RNA molecule is separated from the agent by MIPC. Claim 26 is dependent upon claim 1, which has been amended to recite that the RNA is degraded by MIPC. Therefore, this limitation in claim 26 is redundant. Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new rejection.

Applicants claim a method of separation under conditions that are free of multivalent cations. Therefore, applicants claim a genus of conditions that are free of multivalent cations.

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

Applicants recite a method of stabilizing an RNA molecule against degradation. As an essential element, claim 27 recites the limitation that separation is performed under conditions that are free of multivalent cations capable of interfering with polynucleotide separation. However, the instant specification teaches only that conditions that are free of multivalent cations are a preferred embodiment. Furthermore, the specification teaches that the separation

medium is free of multivalent cations and that it is desirable that the medium be prepared by acids wash and/or cation binding agents (page 8, line 3-12). The disclosure of this single condition is not accompanied by a disclosure as to the relative properties of preparing the separation medium by acid wash or by addition of cation binding reagents such that any condition for avoiding interfering with polynucleotide separation can be envisioned. Nor does the prior art disclose relative properties or identifying characteristics of the recited condition. Therefore, there is no actual reduction to practice or clear description of what is required for conditions that are free of multivalent conditions capable of interfering with polynucleotide separation. Given the diversity of conditions and the inability to determine which will also have the essential element, it is concluded that the invention must be empirically determined. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection**

Claim 26 recites the limitation "mRNA degradation" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 26 recites the limitation "the separation" in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 28 recites the limitation "mRNA degradation" in claim 28. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-11, 21, 26-28 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Gjerde et al (US 2003/0165941; see entire document). **This is a new rejection.**

Gjerde et al teach separation of polynucleotides by Matched ion Polynucleotide Chromatography (MIPC) also referred to as HPLC-based ion pairing Chromatography and furthermore by denaturing MIPC (dMIPC) (page 3, paragraph 0023 and paragraph 0030 and page 4, paragraph 0037). Multivalent cations are removed from all aspects (page 11, paragraph 171). DMIPC involves separation in temperatures ranging from 50°C to about 75°C. Samples are applied to separation media such as silica that support non-polar organic polymers or long

chain C1 to C24 hydrocarbon groups bound to inorganic substrate (page 30, paragraph 417-418) and has an average diameter of 1-100 microns (page 28, paragraph 395). The method comprises contacting the separation media with eluting solution A consisting of 0.1 M TEAA pH 7.2 and solution B that consists of 0.1 M TEAA and 25% acetonitrile (page 35, paragraph 0467). The method is performed using computerized controls and a mobile phase flow control means designed to control the flow of solvent and aqueous phases (see e.g. page 7, paragraph 0082-0084). Given that the process involves addition of mobile phase in gradients and multiple steps, the method is best adapted to a batch process (see page 18, paragraph 253). The procedure disclosed by Gjerde et al is the same as that recited in the instant claims and taught in the instant Specification. Therefore, and absent evidence to the contrary, it would reasonably be expected to yield RNA that is substantially free of agents capable of catalyzing degradation of RNA. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Gjerde et al (WO 98/56798; publication date December 17, 1998; see entire reference). **This rejection is maintained for reasons of record in the office action filed 6/3/03 and 2/13/04 and restated below.**

Gjerde et al teach separation of polynucleotides by MIPC wherein multivalent cations are removed from all aspects (page 3, line 17-19). The separation media can be silica and support non-polar organic polymers or long chain C1 to C24 hydrocarbon groups bound to inorganic substrate (page 5, line 1- 17). The separation media has an average diameter of 1-100 microns (page 3, line 23). The present invention can be used in the separation of RNA although for purposes of description, DNA is described (page 9, line 21) and the procedure can be used for batch process (page 5, line 18-25). The method comprises contacting the separation media with eluting solution A, which consists of 0.1 M TEAA pH 7.2 and B, which consists of 0.1 M TEAA and 25% acetonitrile (page 32, line 20-22). The procedure disclosed by Gjerde et al is the same as that recited in the instant claims and taught in the instant Specification. Therefore, and absent evidence to the contrary, it would reasonably be expected to yield RNA that is substantially free of agents capable of catalyzing degradation of RNA. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim 33 is rejected under 35 U.S.C. 102(e) and 102(a) as being anticipated by Gjerde et al (US 5,972, 222; filed June 10, 1997 and published October 26, 1999; see entire reference). **This rejection is maintained for reasons of record in the office action filed 6/3/03 and 2/13/04 and restated below.**

Gjerde et al teach separation of polynucleotides by MIPC (column 3, line 15-17) multivalent cations are removed from all aspects (column 2, line 43-45). The separation media can be silica and support non-polar organic polymers or long chain C1 to C24 hydrocarbon groups bound to inorganic substrate (column 2, line 63 to column 3, line 2 and column 16, line 40). The separation media has an average diameter of 1-100 microns (column 2, line 31). The present invention can be used in the separation of RNA although for purposes of description, DNA is described (column 5, line 11-20) and the procedure can be used for batch processes (column 3, line 22). The method comprises contacting the separation media with eluting solution A consists of 0.1 M TEAA pH 7.2 and B which consists of 0.1 M TEAA and 25% acetonitrile (column 14, line 45-67 and column 15, line 65 to column 16 line 10). The procedure disclosed by Gjerde et al is the same as that recited in the instant claims and taught in the instant Specification. Therefore, and absent evidence to the contrary, it would reasonably be expected to yield RNA that is substantially free of agents capable of catalyzing degradation of RNA. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim 33 is rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Gjerde et al (US 5,986,085; filing date April 25, 1997 and publication date November 16, 1999; see entire

reference). **This rejection is maintained for reasons of record in the office action filed 6/3/03 and 2/13/04 and restated below.**

Gjerde et al teach a batch process for obtaining polynucleotides from a mixture of polynucleotide fragments (abstract) such as RNA (column 3,line 24-36). A counterion such as TEAA is preferred (column 3, line 37-43). Multivalent cations are removed from all aspects (column 2, line 43-45). The separation media can be silica and support non-polar organic polymers or long chain C8 to C24 hydrocarbon groups bound to inorganic substrate (column 5, line 48- 62). The separation media has an average diameter of 1-100 microns (column 6, line 2). The present invention can be used in the separation of RNA although for purposes of description, DNA is described (column 5, line 11-20) and the procedure can be used for batch process (column 3, line 22). The method comprises of contacting the beads and polynucleotides with and then contacting the separation media with eluting solution such as 0.1 M TEAA pH 7.2 and a gradient of 33%-55% acetonitrile (column 10, line 65-67). The procedure disclosed by Gjerde et al is the same as that recited in the instant claims and taught in the instant Specification. Therefore, and absent evidence to the contrary, it would reasonably be expected to yield RNA that is substantially free of agents capable of catalyzing degradation of RNA. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 7-10, 26, 28 and 33 rejected under 35 U.S.C. 102(a) as being anticipated by Oefner (US 6,453,244 B1; see entire reference). **This rejection is maintained for reasons of record in the office action mailed 2/13/04 and restated below. Upon reconsideration , this rejection has been applied to claim 26 and 28.**

Given that MIPC also referred to as HPLC-based ion pairing Chromatography is defined in the instant specification as a process for segregating RNA using non-polar reverse phase media wherein the process uses a counterion and an organic solvent (see page 11, line 11-14), the method of Oefner et al can be considered to be MIPC. Oefner teaches elution of RNA with a mobile phase containing an ion-pairing reagent and organic solvent under denaturing conditions such as heat or chemicals (see e.g. abstract). Specifically, Oefner teaches isolation using ion pairing reverse phase HPLC in the presence of a counterion and organic solvent (see column 11, line 65 through column 12, line 12). The solid support is comprised of silica and the mobile phase is comprised of TEAA and acetonitrile (see e.g. column 4, lines 7-29). Denaturing conditions include temperatures up to 70°C to 80°C (see e.g. column 4, line 46-53). The separation media has an average diameter of 1-100 microns (column 11, line 24-25), the concentration of TEAA is about 0.05 to 1.0 Molar and about 25% acetonitrile (see e.g. column 12, line 31-55). The present invention can be used in the separation of RNA (see e.g. column 13, line 1-20) and the procedure can be used for large numbers of samples to be analyzed (see e.g. column 14, line 40-48). Columns comprised of PEEK are used (see e.g. column 8, line 28-45). The procedure disclosed by Oefner et al is the same as that recited in the instant claims and taught in the instant Specification. Therefore, and absent evidence to the contrary, it would reasonably be expected to yield RNA that is substantially free of agents capable of catalyzing

degradation of RNA. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim 7-10 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Joachimiak (ABRF News, December 1992; see entire document). **This rejection is maintained for reasons of record in the office action mailed 2/13/04 and restated below.**

Joachimiak teaches large-scale purification of RNA on columns using non-polar silica separation medium (i.e. C18 or C8). For separation, silica gels are used in the presence of ion-pairing reagent and organic solvent such as 0.1 M TEAA in an acetonitrile gradient (see e.g. page 3, paragraph 1-2). Denaturing conditions include temperatures up to 60 °C or 7M urea or high pH (see e.g. page 3, paragraph 1). The procedure disclosed by Joachimiak is the same as that recited in the instant claims and taught in the instant Specification. Therefore, and absent evidence to the contrary, it would reasonably be expected to yield RNA that is substantially free of agents capable of catalyzing degradation of RNA. Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the

same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Response to Arguments

Applicants traverse the claim rejections under 35 USC 102(e) as anticipated by Gjerde WO 98/56798 and US 5,972,222 on page 14-17 of the amendment filed 5/10/04. Applicants argue that the preceding references have been incorporated by reference into the instant application. It is noted that rejections of claims under 102(e) as anticipated by Gjerde et al (US 5,986,085) was included in the discussion.

Applicant's arguments filed 2/13/04 have been fully considered but they are not persuasive. Incorporation by reference does not constitute a benefit claim under 119(e). Accordingly, the fact that WO 98/56798 and US 5,972,222 have been incorporated does not bar there use as prior art references. What governs the use of the references is the priority claim of the instant application, which does not claim benefit to these documents. The instant invention rather has an effective filing date of 3/9/2000 and 6/23/2000 based upon a claim of benefit to respectively 60/187,974 and 60/213,948. Gjerde et al (US 5,972,222) constitutes 102(e) prior art based upon an effective filing date of provisional applications 60/049,123 and 60/063835 of 10/30/97 and constitutes 102(a) art based upon a publication date of 10/26/1999. Gjerde et al (WO 98/56798) constitutes 102(b) art based upon a publication date of 12/17/1998.

Applicants traverse the claim rejection under 35 USC 102(a) as anticipated by Oefner (US 6,453,244) on pages 18-20 of the amendment filed 5/10/04. Applicants argue that the instant specification teaches use of MIPC which does not require a separate pretreatment

denaturing step, and is useful in determining the RNA molecules having lengths exceeding 100-20,000 nucleotides. Oefner does not teach use of MIPC nor use of RNA molecule exceeding 100 nucleotides nor that the RNA molecules as a result of the method are stable. Furthermore, Oefner et al teaches a separate pretreatment denaturation that is not required of MIPC.

Applicant's arguments filed 5/10/04 have been fully considered but they are not persuasive. While applicants have argued that the instant invention uses MIPC and that RNA greater than oligos of 100-200 nucleotides are used in accordance with the instant methods but does not require a separate denaturation step and, these limitations have no express basis in the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). During prosecution, claims must be interpreted as broadly as their terms reasonably allow. Applicants would like to rely on descriptions of the invention that are not reasonably applied to the claims as written. Oefner teaches the isolation of RNA molecules using ion pairing reverse phase HPLC in the presence of a counterion and organic solvent (see column 11, line 65 through column 12, line 12). The difference between the recited method and the prior art is unclear. Therefore, absent evidence to the contrary, the methods of Oefner et al should generate RNA that is stabilized against degradation.

Applicants traverse the claim rejection under 35 USC 102(b) as anticipated by Joachimiak (ABRF News) on pages 20-21 of the amendment filed 5/10/04. Applicants argue that the instant invention has been clarified by incorporation of the limitations of claim 5 into claim 1. In the previous office action, claim 5 was found allowable in view of Joachimiak.

Applicant's arguments filed 5/10/04 have been fully considered but they are not persuasive. The limitations of claim 5 have not been incorporated into claims 7-10 and 33 and therefore these claims remain rejected in view of Joachimiak.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 4-6 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oefner (US 6,453,244 B1; see entire reference) in view of Petro et al (6,260,407; see entire reference). **This is a new rejection.**

Applicants claim a method for stabilizing an RNA molecule against degradation in which a solution of RNA and an agent capable of degrading the RNA and a counter ion are applied to a non-polar separation surface. The RNA is eluted from the separation medium by a mobile phase comprising an organic solvent in which the mobile phase is controlled by a mobile phase flow control using MIPC.

The teachings of Oefner are described above and are applied as before except; Oefner does not teach a mobile phase control means that is controlled by a computer.

Petro et al teaches that the mobile phase of a liquid chromatography system is controlled by a flow control means, which in turn is controlled by a computer. Specifically, the mobile

phase solutions are stored in reservoirs and have dedicated pumps that are controlled by computer (see e.g. figure 6 and bridging paragraph column 37-38).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the computer controls taught by Petro et al with the method of separation of RNA molecules taught by Oefner because Oefner teaches that it is within the ordinary skill of the art to separate RNA using non-polar separation medium in which a mobile phase is passed through to elute RNA and because Petro et al teach that it is within the ordinary skill of the art to control the mobile phase using control means and computers. One would have been motivated to do so in order to receive the expected benefit of generating a high-throughput automated sampling system (see Petro et al, e.g. abstract). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 11 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oefner (US 6,453,244 B1; see entire reference) in view of Petro et al (6,260,407; see entire reference) further in view of Sheridan and Sheridan (Scientist 3(4):23 Feb 20, 1989; see entire document. **This is a new rejection.**

Applicants claim a method for stabilizing an RNA molecule against degradation in which a solution of RNA and an agent capable of degrading the RNA and a counter ion are applied to a non-polar separation surface. The RNA is eluted from the separation medium by a mobile phase comprising an organic solvent in which the mobile phase is controlled by a mobile phase flow control using MIPC under conditions free of multivalent cations.

The teachings of Oefner and Petro et al are described above and are applied as before except; neither Oefner nor Petro teach that conditions of separation are free of multivalent cations.

Sheridan and Sheridan et al teach a Metal-Free column system for use in chromatography in which the recovery of biopolymers is improved (see e.g. page 2, paragraph 5). Sheridan and Sheridan use for example PEEK (polyether ester ketone), which is a non-metal polymer (page 2, paragraph 5). Metals are considered the source of multivalent cations.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the conditions taught by Oefner with the metal-free conditions taught by Sheridan and Sheridan because Oefner teach that it is within the ordinary skill of the art to use PPEK columns for separation of RNA and because Sheridan and Sheridan teach that it is within the ordinary skill of the art to use metal-free conditions in chromatography. One would have been motivated to do so in order to receive the expected benefit of improved recovery that occurs with metal-free conditions. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

Claims 1-2, 4-11, 21, 26-28 and 33 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

July 13, 2004

GERRY LEFFERS
PRIMARY EXAMINER